Appendix 1: Supplementary material

Population and Study design

The screening protocol, enrollment criteria, LDCT settings, and diagnostic algorithm have been previously described [1, 2].

Briefly, between October 2004 and October 2005, 5203 asymptomatic high-risk individuals (smoking history of 20 or more pack-years) aged 50 years or more were enrolled in our single-center trial (COSMOS) and underwent baseline LDCT screening for lung cancer. This single-centre study was approved by the ethics committee of our institute. All recruited volunteers gave written consent to annual LDCT for 10 consecutive years.

Patients with non-calcified nodules detected at baseline or new nodules of 5 mm or less detected at annual screening were scheduled for repeating CT 1 year later. Patients with nodules between 5.1 and 8 mm were scheduled for repeating CT 3 to 6 months later. Patients with nodules greater than 8.1 mm, or growing lesions less than 8mm after repeated scan, were scheduled for PET-CT. Further investigations (repeat LDCT 6 months later, PET-CT, or surgical biopsy) for patients with growing nodules at subsequent annual screening depended on nodule density (non-solid, solid, or partially solid), growth rate and size.

Evolution of diagnostic protocol algorithms for the management of pulmonary nodules detected at baseline CT screening from the beginning of the study until the 10^{th} year of screening trial has been described [3].

Low-dose CT protocols

During the 10 years of CT screening, LDCT scans were performed using 3 different scanners with 8-, 16- and 64-detector rows (Lightspeed Ultra, Lightspeed 16, Optima CT660; GE Healthcare - Waukesha, Wisconsin, USA).

Protocol parameters for both Lightspeed Ultra and Lightspeed 16 were: 120 kVp, 30 mA, rotation time of 0.8 s, 20mm collimation with 2.5mm slice thickness (1.25mm retro-reconstruction). Pitch is slightly different, being 1.675 for Lightspeed Ultra and 1.75 for Lightspeed 16. $CTDI_{vol}$ reported by the scanners are 1.21 mGy and 1.28 mGy for the 8 slice scanner and the 16 slice scanner, respectively.

Acquisitions with Optima CT660 had the following parameters: 120 kVp, 30 mA, revolution time of 0.5 s, pitch 1.375, 40mm collimation with 2.5mm slice thickness (1.25mm retro-reconstruction). The reported $CTDI_{vol}$ was 0.91 mGy.

$CTDI_{vol}$ were measured according to the AAPM Report n.96 [4] to verify that the measured values were within ±10% of the console displayed $CTDI_{vol}$.

PET-CT scan

Images were acquired with a combined PET-CT in-line system (Discovery ST and Discovery 600, GE Medical Systems) consisting of an Advance NXi PET scanner and an 8-slice Light Speed Plus CT scanner. 4 MBq/kg of 18-fluoro-deoxy-glucose were administered intravenously. CT settings were 120 kVp and mA according to body size. PET acquisition time was 3 min per table position. Three-dimensional PET image datasets were reconstructed iteratively, with segmental correction for attenuation using the CT data.

1. Veronesi G, Bellomi M, Veronesi U, et al. Role of positron emission tomography scanning in the management of lung nodules detected at baseline computed tomography screening. *Ann Thorac Surg*. 2007;84(3):959-965.

2. Veronesi G, Bellomi M, Mulshine J, et al. Lung cancer screening with low-dose computed tomography: a non-invasive diagnostic protocol for baseline lung nodules. *Lung Cancer*. 2008;61(3):340-349.

3. Veronesi G, Bellomi M, Scanagatta P, et al. Difficulties encountered managing nodules detected during a computed tomography lung cancer screening program. *J Thorac Cardiovasc Surg*. 2008;136(3):611-617.

4. AAPM Report 96. The Measurement, Reporting, and Management of Radiation Dose in CT. 2008.